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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 07/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/993,287	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 39-46* is/are pending in the application.

4a) Of the above claim(s) *39-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1 and 39-46* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicants response filed May 9, 2005 is acknowledged. In the amendment filed therein, claims 1, 39 and 44-46 were modified. Claims 2-38 have been canceled without prejudice or disclaimer.

Claim Status

2. Claims 39-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10 December 2004.

3. Currently claim 1 is under consideration.

4. Rejections and/or objections of record not reiterated herein have been withdrawn.

OBJECTIONS WITHDRAWN

Information Disclosure Statement

5. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the Examiner on form PTO-892 or Applicant on form PTO-1449 has cited the references they have not been considered.

6. The information disclosure statements filed 3/12/02 and 9/29/03 have been considered as to the merits prior to first action.

Response to Arguments

Applicant contends that the references cited within the specification but not included in the IDS were merely provided for general information and are not deemed pertinent to the patentability of the claimed invention. Accordingly the objection of the IDS is withdrawn.

Oath/Declaration

7. A new oath or declaration is required because the date for Dr. John Marshall (inventor 2) is omitted. The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmations have not been made or if it has not been properly subscribed to, a new oath or declaration is required. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

Response to Arguments

Applicants have submitted a new Oath/Declaration to correct the noted deficiency therein obviating the objection. The objection is withdrawn.

Specification

8. The use of the trademarks has been noted in this application. (.i.e. SEPHAROSE on page 41 lines 4 and 5, TRITON on page 42 line 12). They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Abstract

9. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited.

The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

10. The instant application includes legal phraseology "said". Appropriate correction is required.

Response to Arguments

Applicants have corrected all the items listed in numbers 8, 9, and 10 above via amendment. Therefore the objections are withdrawn.

Please Note: The rejections of record under 35 USC § 112 and 35 USC § 101 have been withdrawn because of the newly amended subject matter. The claims no longer read on sequences consisting of SEQ ID NO:1. New claim 1 reads on sequences (comprising) SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3. Specifically, claim 1 is currently in Markush format reading on sequences including the recited sequences. Therefore the claim is interpreted to read on open transitional phrases, such as comprising.

NEW GROUNDS OF REJECTION NECESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1 does not include a proper transition phrase "comprising" or "consisting of" in the claim. Accordingly it is not clear as to what the sequence will encompasses. As recited the metes and bounds of the claims cannot be determined and one of ordinary skill in the art would not be appraised of the scope of the instant invention. The claim is in the proper Markush Format reciting –selected from the group consisting of.

However this language provides closed interpretation between SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3; it does not clearly identify Applicants intended scope for SEQ ID NO:1, SEQ ID NO:2 and SEQ ID NO:3. It is suggested that the appropriate transition phrase be added to the claim in order to obviate this rejection.

For example, an isolated biopolymer marker selected from the group consisting of sequences comprising SEQ ID NO:1, comprising SEQ ID NO:2, and comprising SEQ ID NO:3. Appropriate correction is required.

Please Note: The rejections under 35 USC 101 and 35 USC 112, 1st paragraph are drawn to sequences comprising SEQ ID NO:3.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

12. Claim 1 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, credible or asserted utility or a well-established utility.

Claim 1 is drawn to a biopolymer marker comprising of SEQ ID NO:3. While the specification asserts that SEQ ID NO:3 has utility as a link or is associated with Type II diabetes. The specification also teaches that the biopolymer marker is useful in methods determining the differential expression (absence, presence, or regulation) of SEQ ID NO:3, wherein a difference from control samples indicates that the sequence is associated with or linked to Type II diabetes.

These methods include for example biopolymer evidencing, characterization, regulation, risk-assessment, and therapeutic identification. The specification also contemplates the use of these methods for diagnosing, staging, monitoring, prognosticating or determining predisposition to Type II diabetes.

Applicant also sets forth figures/drawings as evidence of SEQ ID NO:3 is associated with or linked to Type II diabetes. However, the figures do not identify SEQ ID NO:3 (which band corresponds to sequence identification number 3) thus a correlation with Type II diabetes is impossible. Further, no clear difference expression let alone up and down regulation of the sequence can be determined from the figure or the specification. The correlation with respect to Type II diabetes is also not evident.

Therefore, SEQ ID NO:3 does not appear to be associated with or linked to Type II diabetes (clearly distinguishing the disease from control or normal patients).

There are no disclosure or working examples that demonstrate the specifically asserted utility and evidences a substantial utility was well established at the time of filing.

The specification does not enable one of ordinary skill in the art to definitively assess the incidence of the disease in a single test sample. Furthermore, Applicants have not provided any disclosure enabling the use of the biopolymer marker with regard to regulating the presence or absence of said sequence. The disclosure is equally lacking any teaching for how the identified sequence will be utilized to identify therapeutic avenues and regulate a disease state.

Accordingly, the specification does not identify a specific, substantial, credible or asserted utility or a well-established utility for SEQ ID NO:3.

There is no disclosure designating how the sequence bound in these methods could be regarded as enabling one of ordinary skill in the art to use SEQ ID NO:3 as a marker associated with or linked to Type II diabetes.

Applicants have not set forth any supporting evidence that suggests that SEQ ID NO:3 is associated with or linked to Type II diabetes. Based on the analysis set forth above the specification does not exemplify sufficient findings that constitute a specific, substantial or credible utility.

Claim 1 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by a specific, substantial or credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Response to Arguments

Applicant arguments against SEQ ID NO:1 are MOOT because sequences comprising SEQ ID NO:1 have been addressed under the art rejections herein. However, the amended claims currently include SEQ ID NO:3, which was free of the prior art. The utility of the newly recited sequence (SEQ ID NO:3) is not provided in the disclosure and therefore prompted the rejection under 35 USC 101 above.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation.

Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

Claim 1 is directed to a biopolymer consisting of SEQ ID NO:3 indicative of Type II diabetes. However, the specification does not support this assertion. The specification (in particular page 46) and figures do not definitively correlate the claimed marker comprising SEQ ID NO:3 to Type II diabetes.

Specifically, the specification recites that biopolymers comprising SEQ ID NO:3 were found or regulated differently in the serum of patients suffering from Type II diabetes on page 46, but the specification does not contain any data supporting this contention and the figures do not identify SEQ ID NO:3 as a link to Type II diabetes. Therefore it is unclear how SEQ ID NO:3 was identified as "notable sequences" or how they were deemed "evidentiary" of Type II diabetes.

There is nothing in the disclosure that would enable one to choose SEQ ID NO:3 as notable sequences among an infinite number of possible proteins or peptides present in a patient sample. There is no correlation between the procedure for screening samples from patients suspected of having a variety of different disease, the presence/absence of SEQ ID NO:3, and the determination, prediction, assessment of Type II diabetes.

Furthermore, Applicants have not provided any disclosure enabling the use of the biopolymer marker with regard to regulating the presence or absence of said sequence. The disclosure is equally lacking any teaching for how the identified sequence will be utilized to identify therapeutic avenues and regulate a disease state. There is no disclosure designating how the sequence could be utilized therein, enabling one of ordinary skill in the art to use the sequences in the diagnostic method.

Applicants have not set forth any supporting evidence that suggests that sequences comprising SEQ ID NO:3 are unique molecular markers for Type II diabetes or any other disease and the prior art teaches that disease markers are highly unpredictable and require extensive experimentation. In other words, SEQ ID NO:3 is not identified in the disclosure or the drawings.

Tascilar et al. (Annals of Oncology 10,Suppl. 4:S107-S110, 1999) reports on diagnostic methods in the realm of disease states, however this review article is relevant to Applicants' claimed invention. It is art known that molecular–based assays are valid tools used in predicting and detecting diseases, however as assessed in the Tascilar review "...these tests should be interpreted with caution...". and "the genetic changes found in sources other than the pancreas itself (blood, stool) should be evaluated prudently".

Furthermore, Tockman et al. (Cancer Research 52:2711s-2718s, 1992) teach considerations necessary for a suspected cancer biomarker (intermediate end point marker) to have efficacy and success in a clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to other oncogenic disorders.

Tockman teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials, see abstract. Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and **if validated** (emphasis added) can be used for population screening (p. 2713s, column 1).

The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease.

"This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point [marker]", see page 2714s, column 1, Biomarker Validation against Acknowledged Disease End Points section. Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials, see page 2716s, column 2, Summary section. Tockman reiterates that the predictability of the art in regards to cancer prognosis and the estimation of life expectancies within a population with a disease or disorder are highly speculative and unpredictable.

The instant disclosure has not addressed the issues taught in the prior art as crucial to the discovery of a biopolymer marker.

The nature of the invention- the invention is directed to disease markers or biopolymers.

The state of the prior art- the prior art of record fails to disclose the particular biopolymers in any disease state.

The predictability or lack thereof in the art- there is no predictability based on the instant specification that the biopolymers are indicative of any disease state including Type II diabetes.

The amount of direction or guidance present- appropriate guidance is not provided by the specification for the claimed biopolymers.

The presence or absence of working examples- working examples are not provided in the specification that exemplify the biopolymers as markers for any disease.

The quantity of experimentation necessary- it would require undue amount of experimentation for the skilled artisan to make and use the biopolymers as claimed.

*The relative skill of those in the art-*the level of skill in the art is high.

The breadth of the claims- as recited, the instant claims are directed to a biopolymer consisting of SEQ ID NO:3 being a diagnostic for Type II diabetes.

While it is not necessary to show working examples for every possible embodiment, there should be sufficient teachings in the specification that would suggest to the skilled artisan that the breadth of the claimed biopolymer is enabled. This is not the case in the instant specification.

In view of the teachings of In re Wands, 8 USPQ2d 1400, it has been determined that the level of experimentation required to enable the breadth of the claims is undue.

Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966).

Therefore, in view of the insufficient guidance in the specification, extensive experimentation would be required to enable the claims and to practice the invention as claimed.

Response to Arguments

Applicant arguments against SEQ ID NO:1 are MOOT because sequences comprising SEQ ID NO:1 have been addressed under the art rejections herein. However, the amended claims currently include SEQ ID NO:3 which was free of the prior art. The utility of the newly recited sequence (SEQ ID NO:3) is not provided in the disclosure and therefore prompted the rejection under 35 USC 112, 1st paragraph above.

Please Note: The rejections under 35 USC 102 are drawn to sequences comprising SEQ ID NO:1 and comprising SEQ ID NO:2.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Harrison et al. US Patent #5,849,297.

Harrison et al. discloses sequences comprising or having SEQ ID NO:1 and SEQ ID NO:2. See GenCore protein search dated 8/5/04. Although the reference is silent with respect to sequences being biomarkers, this is deemed inherent to the biopolymer.

A structure which necessarily functions in accordance with the limitations of a process or method claim anticipates the claim. *In re King* (CCPA 1986) 231 USPQ 136. In other words, the sequences set forth in claim 1 would inherently be markers. A compound and its properties are inseparable. *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963). Applicants sequence identification numbers 1 and 2 are disclosed as sequence identification number 1 in the patent to Harrison et al. Therein the claimed sequence is taught.

II. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Harrison et al. US Patent #6,221,657.

Harrison et al. discloses sequences comprising or having SEQ ID NO:1 and SEQ ID NO:2. See GenCore protein search dated 8/5/04. Although the reference is silent with respect to sequences being biomarkers, this is deemed inherent to the biopolymer. A structure which necessarily functions in accordance with the limitations of a process or method claim anticipates the claim. *In re King* (CCPA 1986) 231 USPQ 136. In other words, the sequences set forth in claim 1 would inherently be markers. A compound and its properties are inseparable. *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963). Applicants sequence identification numbers 1 and 2 are disclosed as sequence identification number 1 in the patent to Harrison et al. Therein the claimed sequence is taught.

Response to Arguments

Applicants arguments with respect to the rejections of record under 35 USC 101 and 35 USC 112, 1st paragraph are MOOT because the claimed scope has been modified to read on sequences comprising SEQ ID NO:1 and SEQ ID NO:2. These sequences are taught in the prior art and have been addressed herein.

15. For reasons aforementioned, no claims are allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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